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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,838	07/21/2006	Dan Peters	2815-0374PUS1	7810

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EXAMINER

JARRELL, NOBLE E

ART UNIT	PAPER NUMBER
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1624

NOTIFICATION DATE	DELIVERY MODE
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12/26/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/586,838	Applicant(s) PETERS ET AL.	
	Examiner NOBLE JARRELL	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 and 44-46 is/are pending in the application.
- 4a) Of the above claim(s) 2-5,7-13,19,20,26-28 and 45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6,14-18,21-25,31,33-42 and 44 is/are rejected.
- 7) ☒ Claim(s) 30,32 and 46 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/21/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's election with traverse of group II in the reply filed on 11/24/2008 is acknowledged. The traversal is on the ground(s) that the restriction groups are arbitrary. This is not found persuasive because each group represents a different core structure that is encompassed by formula I. Each of the groups represents a unique structural query as well.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 2-5, 7-13, 19-20, 26-28, and 45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/24/2008.

Claim Objections

3. Claims 1, 6, 14-18, 21-25, 30-42, and 44 are objected to because of the following informalities: they contain non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 6, 14-18, 21-25, 31, 33, and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 6, 14-18, 21-25, 31, 33, and 44 contain generic formula I. Applicants have possession of the elected group (a compound in which the AZA ring

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is 1,4-diazabicyclo[3.3.2]nonane and variable A' and A" are both pyridazine), but not all compounds encompassed by formula I of claim 1.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii) "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406."

According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement, "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". In re *Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those

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skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

This case was filed before Applicants had a clear idea of the structures encompassing the scope of claims 1, 6, 14-18, 21-25, 31, 33, and 44, other than the specific compounds recited in claims 30 and 32. The specification provides broad areas of future research and speculation, inviting undue experimentation in learning how to use Applicants' invention.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). "It is only a definition of a useful result rather than a definition of what achieves that result." "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d

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1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.").

6. Claims 34-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* binding of compounds where the AZA ring is 1-aza-bicyclo[2.2.2]oct-3-yl (which is not the AZA ring in the elected group), does not reasonably provide enablement for: treatment of eating disorders; treatment of central nervous system disorders (including pain); and prevention of Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) *The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to treatment, alleviation, or prevention of diseases related to modulation of cholinergic receptors or monoamine receptors. Thus, the claims

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taken together with the specification imply that diseases related to modulation of cholinergic receptors or monoamine receptors.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Decker et al. (*Expert Opinion in Investigational Drugs*, **2001**, 10(10), 1814-30) teach that although *in vitro* testing leads one to believe that agonism of nicotinic acetylcholine may be effective, but it is not certain that *in vivo* agonism will lead to meaningful pain relief. Development of compounds with improved safety profiles will require additional investigation of mechanisms underlying beneficial and undesirable effects (section 7, page 1826). This teaching leads one of ordinary skill in the art that prediction of *in vivo* properties from *in vitro* data is unpredictable.

Lin et al. (*Expert Opinion in Therapeutic Patents*, **1998**, 8(8), 991-1015) teach that although several compounds that act as modulators of nicotinic acetylcholine have entered clinical evaluation, none have convincingly demonstrated clinical efficacy. Obstacles for successful drug developments are one, ability to show selectivity for nicotinic acetylcholine receptors, two, understanding of what is deemed as a desirable compound profile, and three, a better understanding of the subtypes (section 5, page 1009).

Crow (*expert Opinion in Investigational Drugs*, **1997**, 6(4), 427-36) teach that eating disorders cannot be treated (section 7, pages 433-34).

Pulley et al. (US7067507, issued June 27, 2006) teach that currently Alzheimer's disease cannot be halted, prevented, or reversed (column 2, lines 40-44).

(5) The relative skill of those in the art:

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Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in treatment, alleviation, or prevention of diseases related to modulation of cholinergic receptors or monoamine receptors.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for *in vitro* binding of compounds where the AZA ring is 1-aza-bicyclo[2.2.2]oct-3-yl (which is not the AZA ring in the elected group).

However, the specification does not provide guidance for treatment, alleviation, or prevention of diseases related to modulation of cholinergic receptors or monoamine receptors.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 34-42 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 34-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 34-35 are indefinite in terms of the disorder(s) that is/are being treated,

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alleviated or prevented. It is clear from the specification that nicotine acetylcholine (a cholinergic receptor) is being modulated. However, it is unclear as to what monoamine receptors are being modulated ("Biogenic Monoamines", http://www.nlm.nih.gov/cgi/mesh/2008/MB_cgi?mode=&index=14697&field=all&HM=&II=&PA=&form=&input=, accessed December 12, 2008). Because claims 35-42 are dependent on claim 34, these claims are rejected as well. In claim 37, what cognition disorder is being treated, alleviated, or prevented ("MeSH result", <http://www.ncbi.nlm.nih.gov/sites/entrez>, accessed December 15, 2008)? In claim 42, what "benzodiazepine-like drugs" are being referred to?

9. Regarding claims 36, 38, 40, and 42, the phrase "such as" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

10. Regarding claims 37 and 39, the phrase "including" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Conclusion

11. Claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. The elected group appears free of the prior art of record. Christopoulos et al. (*The Journal of Pharmacology and Experimental Therapeutics*, **2001**, 298 (3), pages 1260-68, cited in IDS) teach compound NNC 11-1607 (page 1261). This compound does not anticipate or render obvious a compound of the elected group because variable L is phenylene, the AZA rings are quinuclidine attached to the rest of the structure at the 3-position, A' and A'' are 1,2, 5-thiadiazole, and variables Y' and Y'' are each OCH₂-ethynylene.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624**